Krebsprädispositionssyndrom-Register 01

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Information for parents/guardians

Liquid Biopsy as a part of

Cancer-Predisposition-Syndrome-Registry-01

Dear Parents/Guardians,
The physician of your child has informed you that your child has been diagnosed with a cancer predisposition syndrome (CPS). One main feature of this genetic condition is an increased cancer risk.

You have already agreed to your child's participation in the cancer predisposition syndrome register 01.

In order to detect CPS-associated malignancies as early as possible and to improve the monitoring of the course of malignant processes, we want to support the establishment of the so-called Liquid Biopsy. This involves the detection of small fragments of the genetic information (DNA) of tumors and other biomarkers in blood.

Within this research project we pursue the following aims:

- We want to understand in which cases of CPS circulating tumor DNA and other biomarkers can be detected and whether liquid biopsies are suitable for the diagnosis, early detection and progression of tumors. Further if Liquid Biopsy is functional as a diagnostic tool for the follow-up care of cancer patients.
- We want to identify the occurrence of malignant processes as early as possible. By detecting tumors at an early stage, the intensity of therapy should be minimised in long term.
- By comparing the results with the early detection tests recorded in CPS-R01, we hope to be able to draw conclusions about the temporal relationship between markers measurable in blood and the occurrence of physical symptoms, radiological evidence of a tumor or changes in other laboratory values.

- We want to establish early detection strategies, which are characterized by high-effectiveness, low-invasiveness and therefore as uneventful as possible. This should lead to a greater willingness to undergo regular checks.

Brief Overview

Current state of knowledge: In recent years, it has become increasingly possible to detect smallest fragments of the genome of healthy cells, but also of tumor cells and other cancer-associated biomarkers in the blood. The analysis of this so-called Liquid Biopsy should make it possible to detect the development and progress of malignancies early and with as little invasiveness as possible. In the future, it is imaginable that this form of liquid diagnostics will also be used for therapy monitoring and aftercare. In addition, there are other markers measurable in the blood that can predict the presence of a tumor. This blood-based and less invasive form of cancer detection is particularly promising for patients with a cancer predisposition syndrome.

Study design: Within this study we are collecting blood of patients with underlying CPS every 6 months, to analyse the samples for freely circulating tumor-DNA. The results of these checks will be compared with the results of the screening tests recorded in CPS-R01.

Procedures and processes: Blood samples should be taken every 6 months and, if possible, as part of other diagnostic or routine blood draws that are normally completed for your child's medical care. For children, approximately 10 ml per blood sample is required, for adults - if possible - 45 ml of blood should be collected. The blood samples are processed at the Clinic for Paediatric Haematology and Oncology at Hannover Medical School and at the Hopp Children's Tumor Centre in Heidelberg. The findings are transferred to the CPS Registry. Since this is a long-term investigation that addresses the course of a condition over several years, the study has no defined duration.

The Risks and Benefits of Participation

Expected individual benefit:
Donating your child's biospecimen and medical data will not necessarily lead to a direct benefit to your child. Our analysis serves primarily as scientific research and is not intended as actionable conclusions for your health. Nevertheless, the research may lead to findings that may be of importance to your child's health. In the situation, when an analysis reveals evidence of a severe previously unknown condition, that can potentially be treated or prevented, we may want to contact you in order to give you this information (see below).

In case you do not wish to receive this type of feedback, please check the box containing "no" on the informed consent. Any time, you can change your decision for or against this feedback option by letting us know. However, please note that you may be obligated to disclose health related information that you receive through our registry, if you prefer this option, to other parties such as health- or life insurance companies. This may be a disadvantage for your child.

The statement above is also relevant to genetic analyses and the discovery of genetic conditions. Therefore, this information may be relevant for your child's family members and family planning.

In the long-term, biospecimen and data collected through our registry is meant eventually to improve the care of patients with cancer predisposition syndromes, which contains DNA repair defects (possibly including participants of the registry). For example, we would like to explore the role of regular evidence-based surveillance strategies and if they may be improved by using liquid biopsies.

General Benefit of the Registry:
Medical studies of this kind aim at a better understanding of the processes associated with disease development and improvement in diagnosis and care. Other patients with a cancer predisposition syndrome not participating in this research may benefit from our findings because our research aims at improving the care of all affected patients. Through the collection of biospecimen from individuals with a cancer predisposition syndrome, cancer research in general is advanced. There may be benefit for patients with cancer even in the absence of a cancer predisposition syndrome. We know that mechanism playing a role in individuals with a cancer predisposition syndrome may be relevant for cancer patients on the whole. In theory, it is possible that our research contributes to better therapy and prognosis of cancer patients.

Risks and Disadvantages of participation:
We would like to collect approximately 45ml blood every 6 months. If possible, these blood draws should be taken as a part of your child's routine medical care. Apart from the complications that may arise with a blood collection, there are no other physical risks for your child.

Every ascertainment, storage, transfer of data is associated with the risk of breaching the confidentiality of the data (e.g. risk of identifying your person/information), which may be especially relevant for genetic information. It is impossible to entirely exclude this type of risk. This risk increases with the amount of connected data, especially if you are publishing genetic information in the internet on your own. Please see below regarding data and material security.

Purpose of collecting biospecimen:
The biomaterials are firstly prepared and stored at the Clinic for Paediatric Haematology and Oncology at Hannover Medical School. Secondly, the samples are transferred to Hopp Children's Tumor Centre in Heidelberg, where the analysis concerning tumor-DNA is conducted. The biospecimen will be stored for an unlimited time for research purposes.

Protection of your biospecimen and data:
The blood samples are taken to the biobank of the Hanover Medical School and the biobank of the University of Heidelberg where they are stored until the end of the research project. Clinical data will be stored on a server of Medical School Hannover. The initials of the first name and surname, the quarter and year of birth, and the sex are recorded. Full names or dates of birth are not stored. However, through the link to the CPS register, it may be possible for the register team to identify your child. However, personal data can only be viewed by the collecting physician and the registry team. Your child's personal data will not be disclosed to third. All identifying information (name, date of birth, address, etc.) will be replaced by an identification code (pseudonymized).
Only after this process, biospecimen and data will be made available for research. Transfer of identifying information to researchers or others such as insurances und employers does not occur.

The encoded biomaterials and medical data can be transferred to universities, research institutes and researching companies, possibly also abroad, for more precisely defined medical research purposes according to previously defined criteria. It is possible that our registry data will be connected to your child's data in other databases, in accordance with the law. When data is transferred abroad, it may not be possible to maintain the same high level of data protection as in Germany. Biomaterials and data issued to researchers may only be used for the predetermined research purpose and may not be passed on by the recipient for other purposes. Remaining material will be returned to the Hannover Unified Biobank or destroyed.
The prerequisite for the use of biomaterials and data for a concrete medical research project is, in principle, that the research project has been evaluated and approved by an ethics committee.
Publications are written in an anonymized fashion to prohibit identification of individual participants. This implies the situation, if data is entered into scientific online databases. A publication of your child's entire genetic information (genome) is impossible without your explicit written permission.

Financial benefits to you or the biobank:
You will not be paid for allowing us to collect and store your child's biospecimen and data. You will not receive financial or other compensation, should findings resulting from the research on your child's biospecimen become commercially valuable. With the transfer of the biomaterials to the biobank of Hannover Medical School or biobank of University of Heidelberg, they become the property of the CPS-R01 Registry of the German Society of Pediatric Oncology and Hematology. The biobank will only use the biospecimen for research purposes. You authorize the registry to use your child's data for research purposes. Your child's specimen and data will not be sold. However, the biobank can ask researchers for an expense allowance for providing specimen to collaborating researchers.

Other Questions and Concerns

Is it possible that you will be contacted regarding the registry?
On a regular basis, results from your child's medical visits are being forwarded to the registry team. In case of missing data, it could be useful that you are contacted at a later time point in order to request additional information or specimen. Also, this contact could occur to request your permission for connecting your child's data with other databases or in order to give feedback to you or your child's physician on findings that may be relevant to your child's health. You will not be contacted through the registry team directly but through your child's physician or the health care institution that cares for your child.

In case you do not wish to be contacted, please check the box containing "no" on the informed consent.

What is your right of withdrawal from the registry?
Any time and without justification and disadvantages you may withdraw your consent that allows us to use your child's biospecimen and data. In case you withdraw your consent, you may decide whether your child's specimen should be destroyed or be anonymized. In the latter situation, we delete the identification code that allows us to connect a specimen to your child. One has to keep in mind that such an anomymization process cannot entirely exclude the small chance that a specimen can be tracked back to your child. Deletion of data may be limited technically feasibility, however. You can also decide whether your child's already collected data should be deleted or may be further used in anonymised form. Data can only be deleted under the conditions of Art. 17 DSGVO. As soon as the purchase of the biomaterials and

other data relating to your child's person has been deleted (anonymisation), destruction is no longer possible. In addition, data from analyses already carried out can no longer be removed.
In case you would like to withdraw your consent, please contact:

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Is your participation voluntary?
Your child's participation in this registry is voluntary. In case you prefer not to participate, your child will experience no disadvantage.

Where can I get additional information?
Should you have additional questions, please contact your child's physician prior to giving your consent. You can also contact Prof. Kratz or Prof. Pfister. Information regarding findings can be found on www.krebs-praedisposition.de.

We are happy to address your questions.

Sincerely

Christian Kratz, MD Stefan Pfister, MD